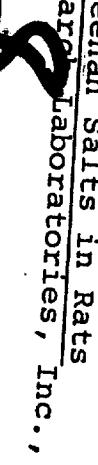


• Teratologic Evaluation of Carrageenan Salts in Rats
and Hamsters' Food and Drug Research
August 31, 1973.



Stauffer Chemical
Company

1-23-74

GKM/5



Stauffer Chemical Company

Westport, Connecticut 06880 / Telephone (203) 226-1511 / Cable "Staufchem"

CARRAGEENAN

The Food and Drug Administration has requested that a statement be prepared on toxicological studies that Stauffer Chemical Company has conducted or sponsored on carrageenan in addition to the studies referred to in the report, "Evaluation of the Health Aspects of Carrageenan as a Food Ingredient", June 1973, SCOGS-6. A statement on these studies follows:

1. Teratologic Evaluation of Carrageenan Salts in Rats and Hamsters, Food and Drug Research Laboratories, Inc., August 31, 1973.

Previous teratology studies had been conducted at the Food and Drug Research Laboratories under contract with the Food and Drug Administration on sodium and calcium salts of carrageenan. A discussion of these studies is contained in the SCOGS-6 Report, pages 6 and 7 and the references cited are (23) and (24).

It was decided to repeat these studies by administering the two carrageenan salts in the diet of the animals instead of administration by intragastric intubation as suspensions in anhydrous corn oil. Accordingly, with the agreement of the Food and Drug Administration, the identical carrageenan samples, identified as FDA 71-3 and FDA 71-5, were fed in the diet of rats and hamsters at two concentrations, 1.0% and 5.0%, during the same fraction of the gestation period in which they were "gavaged" in the previous FDA contracted studies. These studies were jointly sponsored by Hercules, Marine Colloids, and Stauffer Chemical Company.

It was concluded that the ingestion of 1% and 5% by rats of either the sodium or calcium salts of carrageenan had no detectable effect on either maternal or fetal survival, on the rate of nidation, or on the degree of maturation of fetuses. The incidence observed of either soft or skeletal tissue defects did not differ between test groups and the sham-treated controls.

The same conclusion applied to hamsters except that there was a marginally significant reduction in the pregnancy rate of females fed 5% of the calcium salt of carrageenan.

The investigators concluded that neither the sodium or calcium salts of carrageenan was a teratogen for rats or hamsters under the conditions of these studies.

The report of these studies is attached as Appendix A.

2. Ninety Day Study in Rats Using Three Forms of Carrageenan, Institute of Experimental Pathology and Toxicology, Albany Medical College (in progress).

A 90 day feeding study in rats is in progress at the Albany Medical College, sponsored by Stauffer Chemical Company. The study protocol is attached as Appendix B.

In this study, three samples of carrageenan, designated as Carastay® type S (Lot 10036), Carastay® type C (Lot 10236), and Carastay® type AX (Lot 13631), are being fed in concentrations of 1% and 5% in the rat diet. In addition, 5% methycellulose in the diet, is being studied as an experimental control. Rats fed a normal diet are the control animals.

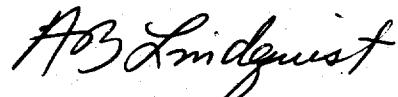
The analytical reports on the three samples of carrageenan being studied in this experiment are attached as Appendix C and Appendix D. They are carrageenan extracts of Chondrus crispus, Kappa-carrageenan. Carastay® type S is the sodium salt, Carastay® type C, the potassium salt, and Carastay® type AX, the calcium salt.

A progress report on the data obtained to date is attached as Appendix E.

Opinions and Recommendations

After a thorough review of the toxicological data available to the Select Committee on Gras Substances and data which have become available since the SCOGS-6 report was written, it is our opinion that there is no evidence in this information that demonstrates that undegraded carrageenan is a hazard to the public health. Undegraded carrageenan and the salts of undegraded

carrageenan are regulated under CFR Title 21 Parts 121.1066 and 121.1067. We recommend that the Food and Drug Administration amend CFR Title 21 Part 121.1066 as proposed in the Federal Register dated August 2, 1972. We further recommend that the opinion of the Select Committee on Gras Substances be reviewed after all data from toxicological studies now in progress have been obtained.

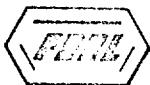


A. B. Lindquist
Manager, Product Regulations

ABL:BA

1/21/74

Appendix A



FOOD AND DRUG
Research LABORATORIES, INC.

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R E P O R T

TERATOLOGIC EVALUATION OF CARRAGEENAN SALTS

IN RATS AND HAMSTERS

Submitted to:

Hercules, Inc.
Wilmington, Delaware

Marine Colloids, Inc.
Rockland, Maine

Stauffer Chemical Co.
Westport, Connecticut

David E Bailey
David E. Bailey, Ph.D.
Manager, Waverly Division

Kenneth Morgareidge
Kenneth Morgareidge, Ph.D.
Vice President

Lab. No. 2004-2005

Date: August 31, 1973



Introduction

In previous studies reported from these Laboratories under contract (No. 71-260) with the Food & Drug Administration, both the sodium and calcium salts of carragheenan had yielded responses in teratology trials which had appeared to be of borderline significance when the test substances were administered by intragastric intubation as suspensions in anhydrous corn oil to rats and hamsters. In evaluating those results, it was pointed out that the so-called "gavage" route of administration entailed a physiological stress which was not imposed when the animals were allowed to consume the test materials as a component of a normal diet.

It was therefore decided to repeat the trials in the same species with these two carragheenates using the identical lots of product originally tested under the code identifications, FDA 71-3 and FDA 71-5 and supplied by the Food & Drug Administration as part of a series of GRAS materials under safety review. However, in conducting the re-tests, it was directed that the compounds be fed in the diet at two concentrations, namely, 1.0 and 5.0 percent during the same fraction of the gestation period in which they were "gavaged" in the previous trials.

This plan was discussed with representatives of the Food & Drug Administration and permission to use portions of the original samples was granted by Dr. Alan Spiher of the Bureau of Foods. The work was sponsored jointly by Hercules, Incorporated; Marine Colloids Company, Inc.; and the Stauffer Chemical Company, Inc.



Experimental

The rats used were Wistar-derived albinos from the closed random-bred colony maintained by these Laboratories. Hamsters were purchased as young adult golden syrians from Lakeview Hamster Colonies. Mating was carried out by caging one male and one female together until a vaginal sperm plug in rats or the presence of motile sperm in vaginal smears in hamsters were observed. The females were then segregated to single cages and that day indicated as Day 0 of gestation. Food (Purina Laboratory Chow) and tap water were supplied ad libitum.

Beginning on Day 6 of gestation in both species, the basal diet was replaced with test diet and continued for 10 consecutive days with rats and 5 for hamsters. Body weights of all females were recorded periodically throughout gestation in both species, and terminal sacrifice was scheduled on Day 20 in rats and Day 14 in hamsters. The uterine contents were examined and the numbers of implants, resorptions, live and dead fetuses recorded, as was the average weight of the live pups in each litter. All fetuses were examined grossly for evidence of external abnormalities, and one-third of each litter fixed in Bouin's solution for examination by the Wilson procedure. The remaining two-thirds were cleared in potassium hydroxide, stained with alizarin red, and preserved in glycerine for examination under low-power magnification.

In both species, pregnant females were assigned across all experimental groups in rotation until the required number (about 20)



of viable litters were obtained. In addition to the two dietary levels of each carragheenan, concurrent groups received the basal (control) diet and one group each received aspirin by stomach tube at the same levels currently used in positive controls.

Results

To facilitate discussion, the data for both rats and hamsters will be presented in tandem as parts (a) and (b) within each table, respectively. Thus, Table 1 (a-b) summarizes the fate of all animals assigned to each group, by species.

Table 2 (a-b) presents the gross reproduction data and the numbers of implant and resorption sites as well as the pup counts. Careful comparison of these data fails to reveal any significant treatment-related effects, especially when considered against the background information which has accumulated with sham-treated controls of both species over the past two years in these Laboratories. Attention should be directed, however, to the reduced pregnancy rate obtained with hamsters at the high level (5.0%) of calcium carragheenate (FDA 71-5). The total number of pregnancies (as a percent of the number mated) was 68% at 5% dietary concentration as compared with 93% at 1.0% in the diet. The corresponding rate in the sham-controls was 82%. Although this difference cannot be regarded as statistically significant, it may represent an effect of treatment on nidation in the hamster. No such effect was seen in the rats.

Table 3 (a-b) is a summary of the skeletal findings and may be dismissed as showing no evidence of an effect of either test



substance on the maturation of the calcifying tissues. It should be remembered that these fetal specimens represent a degree of prenatal development in which skeletal changes are occurring at a rapid rate. Therefore, the variations seen are largely within the normal range of incidence for each category and do not represent terata in any sense.

In table 4 (a-b) are listed the soft-tissue and gross findings, none of which represent unusual aberrations since they were scattered and seen in only a single member of any litter.

The average body weights of the gestating dams are summarized in table 5 (a-b). The individual litter data for each dam are presented in appendices (I and II).

Conclusions

On the basis of the evidence presented herein, it was concluded that the ingestion by rats, during the mid-trimester of gestation, of diets containing as much as 5% of either the sodium or calcium salt of carragheenan has no detectable effect on either maternal or fetal survival, on the rate of nidation, or on the degree of maturation of fetuses. The incidence seen of either soft or skeletal tissue defects did not differ between the test groups and the sham-treated controls.

The same conclusions apply to hamsters except that there was a marginally significant reduction in the pregnancy rate of females fed 5% of the calcium salt in the diet. Under the conditions of the experiment, neither material was a teratogen for rats or hamsters.

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups: A through FMaterial: FDA 71-3 & 71-5

Table 1a

Fate Summary
(Rats)Laboratory No.: 2004

Group	Material	Dose ** per cent	Total		Surviving at Term	
			Mated	Pregnant	Total	Pregnant ¹
A	Control	0.0	25	23	25	23
B	Aspirin*	250.0 mg/kg	25	22	25	22
C	FDA 71-3	1.0	25	24	25	24
D	FDA 71-3	5.0	25	22	25	22
E	FDA 71-5	1.0	25	22	25	22
F	FDA 71-5	5.0	25	21	25	21

* Positive Control : 250.0 mg/kg

** Administered in the diet (Aspirin (Group B)) administered orally

1) Includes all dams examined at term

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups: A through FMaterial: FDA 71-3 & 71-5

Table 1 b

Fate Summary
(Hamsters)Laboratory No.: 2005

Group	Material	Dose ** per cent	Total		Surviving at Term	
			Mated	Pregnant	Total	Pregnant ¹
A	Sham	0.0	28	23	28	23
B	Aspirin*	250.0 mg/kg	28	26	28	26
C	FDA 71-3	1.0	28	24	28	24
D	FDA 71-3	5.0	27	25	27	25
E	FDA 71-5	1.0	28	26	27	25
F	FDA 71-5	5.0	31	21	29	19

* Positive Control: 250.0 mg/kg

** Administered in the diet (Aspirin (Group B)) administered orally

1) Includes all dams examined at term

Group: A through FMaterial: FDA 71-3 & 71-5

Table 2 a
Reproduction Data
(Rats)

Laboratory No. 2004

Group:	Dose (percent):	A	B	C		D	E		F
		Control	Aspirin**	1.0	71-3	5.0	1.0	71-5	5.0
Pregnancies									
Total No.		23	22	24	22	22	22	21	
Died or Aborted (before Day 20)		0	0	0	0	0	0	0	
To term (on Day 20)		23	22	24	22	22	22	21	
Live Litters									
Total No.*		23	20	24	22	22	22	21	
Implant Sites									
Total No.		248	246	269	253	245	245	217	
Average/dam*		10.8	11.2	11.2	11.5	11.1	11.1	10.3	
Resorptions									
Total No.*		2	48	3	4	6	6	8	
Dams with 1 or more sites resorbed		2	9	3	3	4	4	3	
Dams with all sites resorbed		--	2	--	--	--	--	--	
Per cent partial resorptions		8.70	40.9	12.5	13.6	18.2	18.2	14.3	
Per cent complete resorptions		--	9.09	--	--	--	--	--	
Live Fetuses									
Total No.		246	195	266	248	239	239	209	
Average/dam*		10.7	8.86	11.1	11.3	10.9	10.9	9.95	
Sex ratio (M/F)		0.98	1.06	1.06	0.92	0.82	0.82	0.97	
Dead Fetuses									
Total*		--	3	--	1	--	--	--	
Dams with 1 or more dead		--	2	--	1	--	--	--	
Dams with all dead		--	--	--	--	--	--	--	
Per cent partial dead		--	9.09	--	4.55	--	--	--	
Per cent all dead		--	--	--	--	--	--	--	
Average Fetus Weight, g		3.67	2.76	3.83	3.74	3.78	3.78	3.82	

* Includes only those dams examined at term.

** Positive Control: 250.0 mg/kg administered orally

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group: A through FMaterial: FDA 71-3 & 71-5Table 2 b
Reproduction Data
(Hamsters)Laboratory No. 2005

Group:	Dose (percent):	A	B	C	D	E	F
		Control	Aspirin**	1.0	71-3 5.0	1.0	71-5 5.0
Pregnancies							
Total No.		23	26	24	25	26	21
Died or Aborted (before Day 14)		0	0	0	0	1	2
To term (on Day 14)		23	26	24	25	25	19
Live Litters							
Total No.*		23	24	24	25	25	19
Implant Sites							
Total No.		353	413	344	364	386	294
Average/dam*		15.4	15.9	14.3	14.6	15.4	15.5
Resorptions							
Total No.*		16	29	5	2	8	11
Dams with 1 or more sites resorbed		3	8	3	2	3	5
Dams with all sites resorbed		--	1	--	--	--	--
Per cent partial resorptions		13.0	30.8	12.5	8.00	12.0	26.3
Per cent complete resorptions		--	3.85	--	--	--	--
Live Fetuses							
Total No.		331	368	336	360	377	282
Average/dam*		14.4	14.2	14.0	14.4	15.1	14.8
Sex ratio (M/F)		0.64	0.58	0.72	0.64	0.70	0.88
Dead Fetuses							
Total*		6	16	3	2	1	1
Dams with 1 or more dead		1	1	2	1	1	1
Dams with all dead		--	1	--	--	--	--
Per cent partial dead		4.35	3.85	8.33	4.00	4.00	5.26
Per cent all dead		--	3.85	--	--	--	--
Average Fetus Weight, g		1.72	1.68	1.69	1.67	1.73	1.71

* Includes only those dams examined at term.

** Positive Control: 250.0 mg/kg administered orally by intubation

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups A through FLaboratory No. 2004

Table 3a

Material FDA 71-3 & 71-5Summary of Skeletal Findings
(Rats)

Findings	Group No.: Dose (percent):	A		B		C	71-3	D	E	71-5	F
		Control	Aspirin**		1.0	5.0		1.0	5.0		1.0
Live Fetuses Examined, (at term)		175/23		135/20		191/24		171/22	168/22		147/21
Sternebrae											
Incomplete oss.		57/16		46/18		54/16		39/14	44/17		38/14
Scrambled											
Bipartite				6/4					3/3		2/2
Fused											
Extra											
Missing		20/10		106/20		26/10		11/6	17/9		16/9
Other											
Ribs											
Incomplete oss.											
Fused/split				2/2							
Wavy		14/8		64/19		18/11		16/6	20/11		16/9
Less than 12				1/1							
More than 13		2/1		40/11				2/2	1/1		
Other											
Vertebrae											
Incomplete oss.		32/14		102/19		29/14		11/7	18/9		18/12
Scrambled											
Fused											
Extra ctrs. oss.						1/1					
Scoliosis											
Tail defects											
Other											
Skull											
Incomplete closure		30/13		83/19		42/16		20/8	33/13		22/12
Missing				4/4							
Craniostosis											
Other											
Extremities					8/6						
Incomplete oss.											
Missing											
Extra											
Miscellaneous											
Hyoid; missing		15/8		70/16		25/11		10/7	5/5		7/5
Hyoid; reduced		29/14		68/11		23/13		12/6	18/13		21/13

* Numerator=Number of fetuses affected; Denominator=Number of litters affected.

** Positive control: 250.0 mg/kg administered orally

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups A through FLaboratory No. 2005

Table 3 b

Material FDA 71-3 & 71-5Summary of Skeletal Findings
(Hamsters)

Findings	Group No.: Dose (mg/kg):	A		B		C		D		E		F	
		Control	Aspirin**			71-3	5.0			71-5	5.0		
Live Fetuses Examined, (at term)		230/23		251/24		232/24		249/25		260/25		194/19	
Sternebrae													
Incomplete oss.		41/15		125/23		59/17		96/24		88/20		36/14	
Scrambled													
Bipartite		19/12		30/18		23/13		27/16		32/17		28/13	
Fused								1/1					
Extra		2/2				2/1				2/2		1/1	
Missing		43/16		43/20		52/16		73/20		50/12		26/8	
Other													
Ribs													
Incomplete oss.													
Fused/split													
Wavy													
Less than 12													
More than 13		67/22		70/19		78/22		52/18		78/18		54/16	
Other													
Vertebrae													
Incomplete oss.		7/6		8/6		3/2		16/9		12/5		5/3	
Scrambled													
Fused													
Extra ctrs. oss.													
Scoliosis													
Tail defects													
Other													
Skull													
Incomplete closure												1/1	
Missing													
Craniostosis													
Other													
Extremities													
Incomplete oss.		6/3		4/3		6/4		17/8		9/4		1/1	
Missing													
Extra													
Miscellaneous													
Hyoid; missing		3/3		9/4		6/3		7/5		10/5		3/2	
Hyoid; reduced		11/7		8/7		6/5		11/7		8/4		1/1	

* Numerator=Number of fetuses affected; Denominator=Number of litters affected.

** Positive control: 250.0 mg/kg administered orally

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups A through FMaterial FDA 71-3 & 71-5Laboratory No. 2004

Table 4a
Summary of Soft Tissue Abnormalities
(Rats)

Group	Material	Dose Level percent	Dam	Number of Pups	Description
A	Sham	0.0	4005	1	Hydrocephalus
B	Aspirin*	250.0 mg/kg	4035	1	Hydrocephalus
			4042	2	Hydrocephalus
			4050	1	Encephalomyelocele; exophthalmos; hydrocephalus; gastroschisis
C	FDA 71-3	1.0	4079	1	Hydrocephalus
F	FDA 71-5	5.0	4171	1	Hydrocephalus; gastroschisis

* Positive Control: Administered orally 250.0 mg/kg

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups A through FMaterial FDA 71-3 & 71-5Laboratory No. 2005Table 4b
Summary of Soft Tissue Abnormalities
(Hamsters)

Group	Material	Dose Level percent	Dam	Number of Pups	Description
B	Aspirin*	250.0 mg/kg	5041	1	Cleft palate
D	FDA 71-3	5.0	5101	1	Spina bifida; cleft palate; umbilical hernia
E	FDA 71-5	1.0	5144	1	Cleft palate
F	FDA 71-5	5.0	5174	1	Cleft palate

* Positive Control: Administered orally 250.0 mg/kg

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups A through FSpecies Rats

Table 5a

Laboratory No. 2004

Average Body Weights*

Group	Material	Dose Level percent	Day-----				20**
			0	6	11	15	
A	Control	0.0	215	231	251	274	335 (23)
B	Aspirin***	250.0 mg/kg	217	233	244	261	310 (22)
C	FDA 71-3	1.0	224	240	261	284	350 (24)
D	FDA 71-3	5.0	218	235	257	277	339 (22)
E	FDA 71-5	1.0	218	235	256	278	341 (22)
F	FDA 71-5	5.0	209	224	248	266	322 (21)

* Of pregnant dams

** Number of surviving dams in parentheses (c.f. Table 1)

*** Positive control: Administered orally 250.0 mg/kg

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Groups A through FSpecies Hamsters

Table 5b

Laboratory No. 2005

Average Body Weights*

-----Day-----

Group	Material	Dose Level percent	g				14**
			0	6	8	10	
A	Control	0.0	142.5	144.6	153.5	168.7	188.4 (23)
B	Aspirin***	250.0	142.5	144.7	147.9	160.4	185.9 (26)
C	FDA 71-3	1.0	142.3	145.5	154.8	168.9	186.4 (24)
D	FDA 71-3	5.0	140.4	143.8	149.8	164.1	185.2 (25)
E	FDA 71-5	1.0	142.0	146.0	154.4	168.8	190.9 (25)
F	FDA 71-5	5.0	136.1	139.1	146.4	161.1	181.7 (19)

* Of pregnant dams

** Number of surviving dams in parentheses (c.f. Table 1)

*** Positive control: Administered orally 250.0 mg/kg

C

C

C

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group A

Material Control

Dose 0.0 per cent

Appendix I

Reproduction Data in Rats

(Individual)

Laboratory No. 2004

Dam No.	Fate*	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
			Alive	Dead	M	F			
04001	P	11	11		4	7		4.26	
04002	P	8	8		5	3		3.99	
04003	P	8	8		3	5		4.09	
04004	P	11	11		5	6		3.81	
04005	P	11	11		5	6		3.86	
04006	P	11	11		4	7		3.19	
04007	P	9	9		4	5		3.75	
04008	P	8	8		3	5		3.81	
04009	P	12	12		8	4		3.73	
04010	P	6	6		4	2		3.35	
04011	P	11	11		7	4		3.55	
04012	P	12	12		4	8		3.45	
04013	NP	0						----	
04014	P	16	16		11	5		3.86	
04015	P	10	10		6	4		3.73	
04016	P	13	13		8	5		3.14	
04017	P	11	11		4	7		3.80	
04018	P	10	9		3	6	1	3.26	
04019	P	11	11		5	6		3.43	
04020	P	10	9		5	4	1	3.93	
04021	P	14	14		7	7		3.50	
04022	P	11	11		5	6		3.48	
04023	P	14	14		8	6		3.56	
04024	NP	0						----	
04025	P	10	10		4	6		3.79	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group BMaterial AspirinDose 250.0 mg/kg (dosed orally)

Appendix I

Laboratory No. 2004

Reproduction Data in Rats (Individual)

Dam No.	Fate*	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
			Alive	Dead	M	F			
04031	P	10	10		3	7		2.76	
04032	P	12	12		4	8		2.86	
04033	P	12	12		6	6		3.48	
04034	P	13	13		4	9		3.04	
04035	P	14	12		11	1	2	2.57	
04036	P	1	1		0	1		3.65	
04037	P	12	12		10	2		3.25	
04038	P	14	11		4	7	3	3.31	
04039	P	10	9		7	2	1	3.03	
04040	P	13	13		9	4		2.94	
04041	NP	0						----	
04042	P	11	11		6	5		2.95	
04043	NP	0						----	
04044	P	12	2	2	1	1	8	1.55	
04045	NP	0						----	
04046	P	11					11	----	
04047	P	11	6	1	2	4	4	1.92	
04048	P	11					11	----	
04049	P	14	14		8	6		2.97	
04050	P	8	7		4	3	1	2.05	
04051	P	10	10		5	5		2.41	
04052	P	14	14		4	10		3.12	
04053	P	9	9		5	4		2.57	
04054	P	10	3		--**	--**	7	2.26	
04055	P	14	14		6	8		2.42	

* P = Pregnant; NP = Not Pregnant

** Not Recorded

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group CMaterial FDA 71-3Dose 1.0 per cent

Appendix I

Reproduction Data in Rats (Individual)

Laboratory No. 2004

Dam No.	Fate*	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
			Alive	Dead	M	F			
04061	P	9	9		5	4		3.42	
04062	P	13	13		7	6		3.76	
04063	P	11	11		7	4		3.83	
04064	P	13	12		5	7	1	3.97	
04065	P	15	15		10	5		3.68	
04066	P	9	9		4	5		3.92	
04067	P	14	14		6	8		3.45	
04068	P	7	7		5	2		3.93	
04069	P	14	14		6	8		4.04	
04070	P	11	11		4	7		5.32	
04071	P	1	1		1	0		5.28	
04072	P	5	4		2	2	1	4.17	
04073	P	12	12		9	3		3.55	
04074	P	12	12		5	7		3.85	
04075	P	10	10		4	6		3.69	
04076	P	14	14		9	5		3.57	
04077	P	14	14		8	6		3.79	
04078	P	14	14		6	8		3.13	
04079	P	12	12		6	6		3.47	
04080	P	14	14		9	5		3.74	
04081	P	13	13		7	6		3.84	
04082	P	10	10		3	7		3.93	
04083	NP	0						----	
04084	P	13	12		7	5	1	3.30	
04085	P	9	9		2	7		3.40	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group DMaterial FDA 71-3Dose 5.0 per cent

Appendix I

Reproduction Data in Rats (Individual)

Laboratory No. 2004

Dam No.	Fate*	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
			Alive	Dead	M	F			
04091	P	13	13		6	7		3.78	
04092	P	12	12		6	6		3.71	
04093	P	12	12		8	4		3.96	
04094	P	11	11		5	6		3.66	
04095	P	2	2		2	0		4.31	
04096	P	9	7		6	1	2	3.82	
04097	P	12	11	1	6	5		3.67	
04098	P	12	12		6	6		3.20	
04099	NP	0						----	
04100	P	12	12		7	5		4.14	
04101	P	12	12		4	8		3.83	
04102	NP	0						----	
04103	P	11	11		4	7		3.66	
04104	P	13	13		7	6		3.54	
04105	P	8	7		2	5	1	3.53	
04106	P	14	14		5	9		3.37	
04107	P	13	13		5	8		3.91	
04108	NP	0						----	
04109	P	11	11		8	3		3.30	
04110	P	14	14		9	5		5.06	
04111	P	14	13		8	5	1	3.53	
04112	P	11	11		4	7		3.41	
04113	P	12	12		4	8		3.99	
04114	P	12	12		2	10		3.21	
04115	P	13	13		5	8		3.58	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group EMaterial FDA 71-5Dose 1.0 per cent

Appendix I

Reproduction Data in Rats (Individual)

Laboratory No. 2004

Dam No.	Fate*	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
			Alive	Dead	M	F			
04121	P	12	12		4	8		3.21	
04122	P	11	11		6	5		3.78	
04123	P	11	11		2	9		3.73	
04124	P	9	8		4	4	1	3.53	
04125	NP	0						----	
04126	P	11	11		8	3		3.64	
04127	P	10	10		3	7		3.61	
04128	P	14	12		6	6	2	3.70	
04129	P	12	12		5	7		3.57	
04130	NP	0						----	
04131	P	12	12		5	7		4.03	
04132	P	11	11		4	7		3.99	
04133	P	12	12		5	7		3.93	
04134	P	10	10		7	3		3.34	
04135	P	9	7		3	4	2	4.01	
04136	P	15	15		9	6		3.68	
04137	P	11	11		5	6		3.95	
04138	P	11	11		8	3		3.61	
04139	P	11	11		4	7		4.01	
04140	P	10	10		6	4		5.51	
04141	P	10	10		2	8		3.65	
04142	P	12	12		4	8		3.67	
04143	NP	0						----	
04144	P	17	17		7	10		3.55	
04145	P	4	3		1	2	1	3.55	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group FMaterial FDA 71-5Dose 5.0 per cent

Appendix I

Laboratory No. 2004

Reproduction Data in Rats (Individual)

Dam No.	Fate*	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
			Alive	Dead	M	F			
04151	P	10	10		6	4		3.59	
04152	P	8	2		1	1	6	3.01	
04153	P	8	7		3	4	1	3.91	
04154	P	10	10		4	6		3.74	
04155	NP	0						----	
04156	P	13	13		6	7		3.77	
04157	P	11	11		6	5		4.07	
04158	NP	0						----	
04159	P	8	8		6	2		4.42	
04160	P	12	12		6	6		3.87	
04161	NP	0						----	
04162	P	10	10		4	6		3.90	
04163	P	9	8		5	3	1	3.92	
04164	P	12	12		4	8		3.48	
04165	P	15	15		6	9		3.71	
04166	P	9	9		3	6		3.84	
04167	P	10	10		8	2		3.80	
04168	P	9	9		6	3		5.26	
04169	P	11	11		7	4		4.09	
04170	P	10	10		2	8		3.18	
04171	P	10	10		2	8		3.25	
04172	P	11	11		6	5		3.64	
04173	P	10	10		5	5		3.76	
04174	P	11	11		7	4		4.10	
04175	NP	0						----	

* P = Pregnant; NP = Not Pregnant

C

C

C

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group AMaterial ControlDose 0.0 mg/kg

Appendix II

Laboratory No. 2005

Reproduction Data in Hamsters (Individual)

Dam No.	Fate*	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
			Alive	Dead	M	F			
O 5001	NP	0						----	
O 5002	NP	0						----	
O 5003	P	15	15		6	9		1.89	
O 5004	P	12	12		5	7		1.70	
O 5005	P	14	14		3	11		1.59	
O 5006	P	12	12		5	7		1.82	
O 5007	P	14	14		6	8		1.65	
O 5008	P	14	14		7	7		1.61	
O 5009	P	14	14		8	6		1.68	
O 5010	P	16	16		7	9		1.53	
O 5011	P	16	16		7	9		1.80	
O 5012	NP	0						----	
O 5013	NP	0						----	
O 5014	P	13	13		6	7		1.67	
O 5015	P	13	5		0	5	8	1.66	
O 5016	P	13	13		1	12		1.32	
O 5017	P	18	18		3	15		1.89	
O 5018	NP	0						----	
O 5019	P	18	18		4	14		1.87	
O 5020	P	20	7	6	1	6	7	1.63	
O 5021	P	19	19		8	11		1.94	
O 5022	P	15	15		8	7		1.53	
O 5023	P	17	16		6	10	1	1.83	
O 5024	P	17	17		9	8		1.81	
O 5025	P	17	17		9	8		1.84	
O 5026	P	14	14		7	7		1.77	
O 5027	P	15	15		6	9		1.90	
O 5028	P	17	17		7	10		1.67	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group BMaterial AspirinDose 250.0 mg/kg (dosed orally)

Appendix II

Laboratory No. 2005

Reproduction Data in Hamsters (Individual)

Dam No.	Fate*	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
			Alive	Dead	M	F			
O 5031	P	11	9		0	9	2	1.75	
O 5032	P	12	12		4	8		1.75	
O 5033	P	16	16		6	10		1.59	
O 5034	P	14	13		6	7	1	1.69	
O 5035	P	17	16		8	8	1	1.58	
O 5036	P	17	17		8	9		1.46	
O 5037	P	13	13		6	7		1.33	
O 5038	P	22	22		13	9		1.49	
O 5039	P	15	7		2	5	8	1.77	
O 5040	P	17	17		4	13		1.83	
O 5041	P	15	15		8	7		1.66	
O 5042	P	15	15		8	7		1.71	
O 5043	NP	0						----	
O 5044	P	16	16		2	14		1.78	
O 5045	P	16	16		5	11		1.74	
O 5046	NP	0						----	
O 5047	P	20	18		1	17	2	1.78	
O 5048	P	13					13	----	
O 5049	P	15	15		4	11		1.76	
O 5050	P	13	12		5	7	1	1.58	
O 5051	P	16	15		5	10	1	1.60	
O 5052	P	24	24		10	14		1.84	
O 5053	P	16	16		5	11		1.55	
O 5054	P	20	20		10	10		1.83	
O 5055	P	16		16				----	
O 5056	P	17	17		6	11		1.78	
O 5057	P	18	18		6	12		1.72	
O 5058	P	9	9		3	6		1.79	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group CMaterial FDA 71-3Dose 1.0 percent

Appendix II

Laboratory No. 2005

Reproduction Data in Hamsters (Individual)

Dam No.	Fate*	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
			Alive	Dead	M	F			
O 5061	P	13	12		4	8	1	1.87	
O 5062	P	16	16		8	8		1.76	
O 5063	P	14	14		6	8		1.71	
O 5064	P	16	16		6	10		1.56	
O 5065	P	10	10		5	5		1.86	
O 5066	P	17	17		7	10		1.48	
O 5067	P	14	14		7	7		1.54	
O 5068	P	15	13	2	5	8		1.66	
O 5069	P	18	18		11	7		1.61	
O 5070	P	17	17		10	7		1.72	
O 5071	NP	0						----	
O 5072	P	6	6		5	1		1.96	
O 5073	P	13	13		8	5		1.85	
O 5074	P	17	17		9	8		1.50	
O 5075	P	17	17		4	13		1.59	
O 5076	P	14	12		0	12	2	1.35	
O 5077	P	17	15		5	10	2	1.72	
O 5078	NP	0						----	
O 5079	P	14	14		2	12		1.50	
O 5080	P	14	13	1	2	11		1.62	
O 5081	P	13	13		6	7		1.97	
O 5082	P	15	15		7	8		1.64	
O 5083	NP	0						----	
O 5084	P	18	18		7	11		1.57	
O 5085	P	15	15		7	8		2.02	
O 5086	P	13	13		5	8		1.81	
O 5087	NP	0						----	
O 5088	P	8	8		5	3		1.73	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group DMaterial FDA 71-3Dose 5.0 percent

Appendix II

Laboratory No. 2005

Reproduction Data in Hamsters (Individual)

Dam No.	Fate*	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
			Alive	Dead	M	F			
O 5092	P	15	13	2	5	8		1.77	
O 5093	P	15	15		7	8		1.67	
O 5094	NP	0						----	
O 5095	P	14	14		9	5		1.85	
O 5096	P	13	12		5	7	1	1.61	
O 5097	P	13	13		6	7		1.85	
O 5098	P	10	10		4	6		1.47	
O 5099	P	13	13		2	11		1.63	
O 5100	P	15	15		7	8		1.38	
O 5101	P	10	9		5	4	1	1.28	
O 5102	P	17	17		14	3		1.61	
O 5103	P	17	17		11	6		1.83	
O 5104	P	15	15		3	12		1.65	
O 5105	P	13	13		4	9		1.67	
O 5106	P	12	12		4	8		1.88	
O 5107	P	14	14		1	13		1.33	
O 5108	NP	0						----	
O 5109	P	16	16		1	15		1.45	
O 5110	P	21	21		1	20		1.58	
O 5111	P	18	18		7	11		1.59	
O 5112	P	13	13		5	8		1.72	
O 5113	P	17	17		7	10		1.94	
O 5114	P	14	14		6	8		1.83	
O 5115	P	19	19		9	10		1.86	
O 5116	P	13	13		6	7		1.89	
O 5117	P	13	13		5	8		1.79	
O 5118	P	14	14		6	8		1.70	

* P = Pregnant; NP = Not Pregnant

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group EMaterial FDA 71-5Dose 1.0 percent

Appendix II

Reproduction Data in Hamsters (Individual)

Laboratory No. 2005

Dam No.	Fate*	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
			Alive	Dead	M	F			
O 5121	P	13	13		6	7		1.77	
O 5122	P	15	15		7	8		1.88	
O 5123	P	12	12		5	7		1.87	
O 5124	P	18	18		9	9		1.67	
O 5125	P	17	17		8	9		1.75	
O 5126	P	13	13		8	5		2.00	
O 5127	NP	0						----	
O 5128	P	16	16		11	5		1.90	
O 5129	P	13	7		1	6	6	1.30	
O 5130	P	19	19		10	9		----	Aborted Day 14
O 5131	P	18	18		13	5		1.66	
O 5132	P	14	13		8	5	1	1.78	
O 5133	P	12	12		9	3		1.83	
O 5134	P	20	20		2	18		1.45	
O 5135	P	15	14	1	5	9		1.68	
O 5136	P	15	15		4	11		1.68	
O 5137	P	16	16		2	14		1.74	
O 5138	P	18	18		1	17		1.73	
O 5139	P	12	12		3	9		1.52	
O 5140	P	15	15		2	13		1.57	
O 5141	P	17	17		7	10		1.81	
O 5142	P	17	17		6	11		1.96	
O 5145	P	17	17		7**	9**		1.69	
O 5144	P	18	18		10	8		1.72	
O 5145	P	14	14		5	9		1.71	
O 5146	P	15	14		6	8	1	1.87	
O 5147	P	16	16		8	8		1.77	
O 5148	NP	0						----	

* P = Pregnant; NP = Not Pregnant

** Not all recorded

FOOD AND DRUG RESEARCH LABORATORIES, INC.

Group FMaterial FDA 71-5Dose 5.0 percent

Appendix II

Reproduction Data in Hamsters (Individual)

Laboratory No. 2005

Dam No.	Fate*	Implant Sites	Fetuses		Sex		Resorption Sites	Average Fetus Weight (g)	Remarks
			Alive	Dead	M	F			
O 5151	P	13	12		5	7	1	1.72	
O 5152	P	14	14		--	--		----	Aborted Day 14
O 5153	P	17	17		7	10		1.70	
O 5154	NP	0						----	
O 5155	NP	0						----	
O 5156	NP	0						----	
O 5157	NP	0						----	
O 5158	P	16	16		10	6		1.44	
O 5159	P	16	14		9	5	2	1.27	
O 5160	P	14	14		9	5		1.88	
O 5161	P	17	16		11	5	1	1.74	
O 5162	P	16	16		11	5		1.64	
O 5163	P	18	18		9	9		1.51	
O 5164	NP	0						----	
O 5165	P	13	13		6	7		1.84	
O 5166	P	15	9		0	9	6	1.57	
O 5167	P	14	14		--	--		----	Aborted Day 14
O 5168	NP	0						----	
O 5169	NP	0						----	
O 5170	NP	0						----	
O 5171	P	17	17		7	10		1.93	
O 5172	P	18	18		7	11		1.82	
O 5173	P	19	18	1	6	12		1.50	
O 5174	P	15	15		6	9		1.87	
O 5175	P	14	14		6	8		1.99	
O 5176	P	16	16		7	9		1.81	
O 5177	NP	0						----	
O 5178	P	14	13		6	7	1	1.79	
O 5179	NP	0						----	
O 5180	P	13	13		5	8		1.69	
O 5181	P	13	13		5	8		1.80	

* P = Pregnant; NP = Not Pregnant

Appendix B

INSTITUTE OF EXPERIMENTAL PATHOLOGY & TOXICOLOGY
 ALBANY MEDICAL COLLEGE
 ALBANY, NEW YORK 12208

PROTOCOL

NINETY-DAY STUDY IN RATS USING
 THREE FORMS OF CARRAGEENAN

Methods

There will be 4 test groups (Sprague-Dawley rats - Charles River CD 1) comprised of 25 males and 25 females each. Group 1 will be fed normal diet, Group 2 (experimental control) will receive 5% methylcellulose food grade in the diet, Group 3 will receive 1% of the test material in the diet, and Group 4 will receive 5% test material in the diet. The animals, weanling rats weighing approximately 50 g, will be acclimatized for 1 week before use.

<u>Group #</u>	<u>No. of animals</u>		<u>Dosage</u>	<u></u>
	<u>M</u>	<u>F</u>		
1	25	25	normal diet	control
2	25	25	5% methylcellulose in diet	experimental control
3	25	25	1%	Carrageenan A
3	25	25	"	Carrageenan B
3	25	25	"	Carrageenan C
4	25	25	5%	Carrageenan A
4	25	25	"	Carrageenan B
4	25	25	"	Carrageenan C

All surviving rats will be sacrificed at 90-97 days. The tissues will be examined macroscopically and fixed in appropriate fixatives but only the high dose animals in each group and controls will be examined histologically initially.

Hematology will be performed before the start of the experiment and at 90 days, on 10 rats of each dietary level of each group as well as the controls. The investigations will comprise total erythrocyte and leucocyte counts, hemoglobin, hematocrit and differential leucocyte counts.

Clinical chemistry will similarly be performed and will comprise blood glucose, BUN, serum sodium, potassium and chloride, SGPT.

Appendix C

P. O. Box 2357, 169 Front Street
South Portland, Maine 04106
REPORT OF ANALYSIS.

Appendix C

CUSTOMER Dr. Fredrick Coulston

ADDRESS Albany Medical College

47 New Scotland Ave., Albany, N.Y.
12208

DATE July 2, 1973

REF. Stauffer letter of 7-2-73

SHIPMENT OF Carrageenan, Carastay[®] Type S, Type C and Type AX

DATE SHIPPED June 29, 1973

CAR NO. None

ANALYSIS:

This is to certify that Carrageenan, Carastay[®] Type S, Type C and Type AX complies with the specifications of the Food Chemicals Codex, Second Edition.

Determinations	Food Chemicals Codex Specifications	Type S Lot 10036	Type C Lot 10236	Type AX Lot 13631
Ash (Total)	35% maximum	26.3%	29.5%	32.6%
Ash (Acid-Insoluble)	1% maximum	0.90%	0.77%	0.12%
Loss on Drying	12% maximum	6.0%	7.9%	5.9%
Sulfate (Dry weight basis)	20% - 40%	25.6%	23.6%	22.2%
Arsenic (as As)	3 ppm maximum	2.1 ppm	2.8 ppm	2.8 ppm
Heavy Metals (as Pb)	40 ppm maximum	Passes test	Passes test	Passes test
Lead	10 ppm maximum	4 ppm	2 ppm	4 ppm

R. S. Bryant

Manager, Quality Assurance
Industrial Chemical Division

Appendix D

INDUSTRIAL CHEMICAL DIVISION
Westport, Connecticut 06880

Appendix D

REPORT OF ANALYSIS

CUSTOMER Dr. Fredrick Coulston

ADDRESS Albany Medical College

47 New Scotland Ave., Albany, N. Y.

DATE July 19, 1973

REF. Stauffer letter of 7-19-73

ITEM OF Carrageenan, Carastay® Type S, Type C and Type AX

DATE SHIPPED June 29, 1973

CAR NO. None

ANALYSIS:

Carrageenan Extract of
Chondrus crispus

Determination	Type S Lot 10036	Type C Lot 10236	Type AX Lot 13631
Viscosity*	270cps	190cps	26cps
pH (1% Solution)	9.5	9.5	10.1
Calcium (Ca)	0.64%	2.8%	6.1%
Sodium (Na)	5.93%	3.45%	2.6%
Potassium (K)	0.87%	5.7%	1.2%
Ammonium (Expressed as NH ₃)	Less than 0.1%	Less than 0.1%	Less than 0.1%
Kappa Fraction	70.6%	81.4%	87.9%
Lambda Fraction	29.4%	18.6%	12.1%

*1.5% by weight aqueous solution at 75°C as determined by LVF Brookfield viscometer using number one spindle at 30 r.p.m..

Appendix E

Institute of Comparative and Human Toxicology

Albany Medical College

Albany, New York 12208

Preliminary Report on Rats given Carrageenan
Obtained from Stauffer Company

January 17, 1974

Dr. Frederick Coulston
Professor and Director



Dr. Leon Golberg
Professor and Scientific Director

Dr. Rajender Abraham
Project Leader
Associate Professor

Mr. W. Ford
Medical Technologist

Experimental Design:

There are 7 test groups (Sprague-Dawley rats, Charles River CD-1) comprised of 25 males and 25 females each. Group 1 is being fed normal diet, Group 2 receiving 5% Alphacel food grade in the diet, Group 3 thru 5 is receiving 5% of the test materials in the diet, and Group 6 thru 8 is receiving 1% of the test materials in the diet.

Group	# of Animals		Dosage	Test Material
	M	F		
I	25	25	normal diet	control
II	25	25	5% in diet	Alphacel
III	25	25	5% " "	Type AX
IV	25	25	5% " "	Type S
V	25	25	5% " "	Type C
VI	25	25	1% " "	Type AX
VII	25	25	1% " "	Type S
VIII	25	25	1% " "	Type C

The animals, weanling rats weighing approximately 50 gm. were acclimated for 1 week in the animal quarters.

Blood samples for clinical chemistry and hematology were obtained by aortic puncture from 10 male and 10 female rats drawn randomly from the acclimated animal group (Table I, Table II). The clinical chemical and hematologic values of males and females fall within the normal range for animals of that age.

No significant differences in mortality between test groups and control groups at 9 weeks have been observed (Table IV).

IN62 RATS (Stauffer)

Table I. Clinical Chemistry

♂	Rat #	SGPT (SF)	mg/l			mg%	
			Na ⁺	K ⁺	Cl ⁻	BUN	gluc.
	1342	26	147	4.8	102	18	156
	1343	34	146	4.9	104	22	162
	1344	28	145	4.9	106	21	167
	1345	31	145	5.0	111	17	175
	1346	64	145	4.8	109	19	182
	1347	51	144	5.6	107	20	168
	1348	31	145	5.2	qns	→	
	1349	28	144	4.8	98	19	196
	1350	37	144	5.3	101	19	182
	1351	28	143	4.9	104	17	202
	Mean ± S.D.	37±12	145±1	5.0±0.3	105±4	19±2	177±15
♀	1352	33	147	4.8	104	21	176
	1353	37	148	5.0	101	21	160
	1354	34	147	5.2	101	21	173
	1355	43	142	5.2	103	22	182
	1356	27	143	5.9	105	21	188
	1357	34	142	5.0	102	19	172
	1358	37	144	5.0	105	19	166
	1359	34	144	4.7	102	23	180
	1360	28	143	4.9	104	21	174
	1361	31	141	4.6	105	19	164
	Mean ± S.D.	34±5	144±2	5.0±0.4	103±2	21±1	174±9

Species Rat (Weanling) from Aorta

Hematology

Test Period

Day 0

Order

INT# 62 (Stauffer)

Route _____

Notebook W.H. Ford

Date 11/21/74

Table II

No.	Dose	Sex	R.B.C. (X 10 ⁶)	Hemoglobin (gms %)	Hematocrit (%)	W.B.C. (X 10 ³)	DIFFERENTIAL						P.T.T. (Sec)	Platelet (X 10 ⁶)	Protime (Sec)
							Neut	Lymph	Mono	Eos.	Baso	Other			
1342		♂	4.74	10.6	32	5.0									
1343			4.51	11.8	37	4.7									
1344			5.71	11.2	35	5.7									
1345			4.44	12.0	36	5.3									
1346			4.65	11.4	34	6.0									
1347			3.22	11.0	22	3.0									
1348			4.88	10.1	31	4.0									
1349			4.22	11.2	35	5.5									
1350			4.67	11.6	34	4.8									
1351			4.56	11.4	34	3.5									
mean			4.57	11.2	330	4.8									
± S.D.			±0.62	0.6	4	1.0									

Species Rat (Weanlings) from Aorta Hematology Test Period
Route _____ Day 0 _____ Order _____
Notebook W.H. Ford Week _____ INT# 62 (Stauffer)
Month _____ Date 11/21/74

Table III

Table IV

Mortality of Rats given test materials in the diet for 9 weeks

Group	Treatment	# of Rats remaining	
		Male	Female
I	control	25	25
II	alphacel 5%	23	25
III	Type AX 5%	23	24
IV	Type S 5%	24	25
V	Type C 5%	25	25
VI	Type AX 1%	23	25
VII	Type S 1%	24	25
VIII	Type C 1%	25	25

The presence of fecal occult blood was determined by the Hema-test™ method. ~~The results are highly variable, a tabular presentation of 30 determinations per group over a 6 week period are given (Table VI).~~ *1/11/74
ABZ*

The results are highly variable, a tabular presentation of 30 determinations per group over a 6 week period are shown (Table V). Soft stools have been observed in a number of animals from all the test groups.

The body weights of test animals over a nine week period are not significantly different from the control groups (Table VI).

Occult Blood in Rats Given Several Carrageenans in the Diet

Table V

Group	Treatment	male			female		
		+	±	-	+	±	-
I	control diet	14/30	3/30	13/30	7/30	3/30	20/30
II	Alphacel 5%	24/30	3/30	3/30	19/30	4/30	7/30
III	Type AX 5%	15/30	8/30	7/30	15/30	8/30	7/30
IV	Type S 5%	16/30	7/30	7/30	14/30	8/30	8/30
V	Type C 5%	12/30	11/30	7/30	11/30	8/30	11/30
VI	Type AX 1%	16/30	7/30	7/30	21/30	7/30	2/30
VII	Type S 1%	17/30	8/30	5/30	17/30	6/30	7/30
VIII	Type C 1%	21/30	6/30	3/30	10/30	10/30	10/30

Body Weights* of Rats Given Several Carrageenans in the diet for a period of 8 weeks.

Table VI

Sex	Group	0	1	2	3	4	5	6	7	8
Female	I	46±3	78±7	117±10	145±17	168±12	185±13	206±16	225±17	237±21
	II	45±3	75±6	114±8	138±17	150±13	179±11	201±12	218±11	231±12
	III	46±3	76±5	116±11	144±9	167±11	186±13	204±15	222±16	231±18
	IV	45±4	76±6	112±11	147±15	166±10	188±10	207±11	223±11	232±13
	V	47±3	77±7	113±11	144±13	166±11	187±12	207±12	222±16	229±15
	VI	46±4	79±8	115±15	148±15	171±16	188±16	202±19	214±20	224±21
	VII	47±4	78±6	114±11	145±12	171±9	186±11	199±15	215±15	226±16
	VIII	46±6	76±5	115±10	151±10	172±12	191±15	201±18	216±21	228±22
Male	I	52±5	84±6	129±11	170±10	190±25	235±13	279±30	340±22	380±25
	II	54±5	85±10	133±13	159±29	168±28	232±23	288±35	337±34	375±35
	III	51±5	82±8	125±13	164±17	191±21	233±25	279±31	337±30	358±33
	IV	52±4	84±8	121±10	160±22	194±28	236±31	275±44	326±46	360±46
	V	51±5	82±7	125±15	165±25	208±21	239±26	283±31	332±28	368±28
	VI	52±4	85±7	132±17	179±24	217±31	250±37	289±49	333±45	366±46
	VII	51±4	86±6	131±16	184±15	226±15	263±17	308±30	355±23	386±28
	VIII	52±6	83±7	133±15	172±17	217±23	256±28	307±35	351±32	381±34

*average in gm ± 1 S.D.